REMARKS

1. Status of the Claims

Claims 69-72 and 89-96 are pending and under active consideration in this application.

2. 35 U.S.C. §§ 101 and 112, first paragraph

On pages 2-8 of the Office Action, the Examiner rejects claims 69-72 and 89-96 under 35 U.S.C. § 101 for allegedly lacking a credible, specific, and substantial asserted utility, or a well established utility. The Examiner also rejects these claims under 35 U.S.C. § 112, first paragraph for allegedly lacking utility. In view of the Examiner's remarks at pages 7 and 8 of the Office Action, Applicant submits that the only remaining issue is whether the claimed subject matter has a credible utility. In support of Applicant's assertion of credible utility in the July 29, 2008 office action reply (the "Previous Reply"), Applicant presented experimental evidence that validated a biological function for the claimed subject matter. The Examiner now requires that Applicant provide this evidence in the form of a proper and timely filed Declaration. Thus, respectfully submitted herewith is the Declaration of Ayelet Chajut, Ph.D. (the "Chajut Declaration"), which describes the experimental support for credible utility that was presented in the Previous Reply. The results described in the Chajut Declaration are summarized below.

First, both hsa-miR-20b (SEQ ID NO: 2; GAM3298) and hsa-miR-18b (SEQ ID NO: 9; GAM2608) are expressed in Hep3B cells, as shown in microarray experiments supervised and conducted by Dr. Chajut. *The Chajut Declaration*, at items 4 and 5. Second, Dr. Chajut supervised and conducted experiments yielding results that are consistent with an ability of the claimed miRNAs to bind to and regulate their asserted respective targets. *See Id.*, at items 6-12. Specifically, the experiments entailed transfecting Hep3B cells with anti-sense oligonucleotides (ASOs) that are designed to specifically bind to either hsa-miR-20b or hsa-miR-18b, and then comparing the mRNA levels of the respective miRNA targets STAT3 or ATP7A to a control. Messenger RNA levels were measured using quantitative reverse transcription polymerase chain reactions ("qRT-PCR") and expressed as a 50-Ct cycle threshold value. *See Id.*, at item 7. Applicant notes that the Previous Reply erroneously referred to the levels being expressed as "Ct." This was due to a typographical error that Applicant did not notice until preparing the instant reply. Whether mRNA levels are described in "Ct" or "50-Ct" does not change the measure of the relative differences in mRNA expression between miRNA-specific ASO-treated- and control cells described in the Previous Reply and those presented here.

The ASO experiments are based on the prediction that if a miRNA is capable of reducing the levels of a particular target mRNA, an ASO that specifically inhibits the miRNA would cause an increase in target mRNA levels. The experiments described in the Chajut Declaration demonstrate that transfection of the hsa-miR-20b-specific ASO resulted in 1.2-fold increase in STAT3 mRNA levels compared to the control. *See Id.*, at items 8 and 9. Similarly, transfection with the hsa-miR-18b-specific ASO yielded a 1.8-fold increase in ATP7A mRNA levels compared to the control. *See Id.*, at items 10 and 11. These results are consistent with the abilities of hsa-miR-20b and hsa-miR-18b to specifically regulate their respective asserted targets STAT3 and ATP7A. Accordingly, claimed sequences SEQ ID NO: 2 (hsa-miR-20b) and SEQ ID NO: 9 (hsa-miR-18b) are expressed in cells. Additionally, specifically inhibiting the activity of the claimed miRNAs results in increased levels of their target mRNAs. Therefore, the utility of the claimed nucleic acids is firmly established by experimental evidence now on the record.

Moreover, the application as originally filed presented evidence of the actual existence of the claimed miRNAs. Paragraphs 0309-0321 of the specification and Figures 22A and 22B showed that both hsa-miR-20b and hsa-miR-18b were specifically detected in a HeLa cell cDNA library. These portions of the application also established that hsa-miR-20b was cloned and sequenced. Accordingly, the application as filed demonstrated that both miRNAs were expressed in HeLa cells.

In view of the foregoing, Applicant respectfully requests that the Examiner reconsider and withdraw the rejection of the claims under 35 U.S.C. § 101. Additionally, because the claimed nucleic acids are supported by a specific, substantial, and credible utility, Applicant requests that the Examiner reconsider and withdraw the rejection of the claims under 35 U.S.C. § 112, first paragraph.

3. Conclusion

Applicant respectfully submits that the instant application is in good and proper order for allowance and early notification to this effect is solicited. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the instant application, the Examiner is encouraged to call the undersigned at the number listed below.

Respectfully submitted,

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